

J-Glucosyltransferase (J-GT) Null Mutant in *Leishmania mexicana*

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Base J is a unique modified DNA base β -D-glucosyl-hydroxymethyluracil) found in the nuclear genomes of trypanosomatids, *Euglena*, and *Diplonema*. It replaces around 1% of thymidines. Base J biosynthesis occurs in two steps: first, the J-binding proteins JBP1/JBP2 hydroxylate thymidine residues to form 5-hydroxymethyluracil (hmU); second, hmU is glucosylated by a specific J-glucosyltransferase (J-GT) to generate base J. Base J has been implicated in transcription termination, telomere maintenance, and presumably metacyclogenesis. Previously, we demonstrated that inhibition of JBP1/JBP2 thymidine hydroxylase activity by dimethyloxalylglycine (DMOG) reduces base J levels in *Leishmania mexicana* genome, leading to the arrest at the metacyclic stage and impaired *in vitro* differentiation into axenic amastigotes. Ablation of the *J-GT* gene in *Trypanosoma brucei* causes a complete loss of base J. In this study, we generated a J-GT null mutant in *L. mexicana* using CRISPR/Cas9 technology to investigate the effect of the complete loss of the J base on parasite differentiation and infectivity.